AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph at page 12, lines 18-19 with the following replacement paragraph:

Figure 1A: Nucleic acid sequence (~~A,~~ SEQ ID NO: 1) of BACE455. ~~and~~

Figure 1B: Amino ~~amino~~ acid sequence (~~B,~~ SEQ ID NO: 2) ~~sequence~~ of BACE455 and alignment of amino acid sequence with BACE501 (SEQ ID NO: 36).

Please replace the paragraph at page 12, lines 22-28 with the following replacement paragraph:

Figure 2 : ~~BACE455 (A, C) and BACE501 (B, D) immunolocalization~~ Immunolocalization on NIH 3T3 cells transfected with a construct expressing BACE455 or BACE501. ~~A, B:~~ Intracellular staining of BACE isoforms (BACE455, Fig. 2A; BACE501, Fig. 2B) on Triton X100- permeabilized cells using polyclonal anti-hBACE (481-501) (C-ter intracellular epitope). ~~C,D:~~ Extracellular staining of BACE isoforms (BACE455, Fig. 2C; BACE501, Fig. 2D) on non-permeabilized cells using polyclonal anti-hBACE (46-65) (N-ter extracellular epitope). Photomicrograph showing that BACE455 presents similar intracellular localization than BACE501, is efficiently exported to the cellular membrane where it displays comparable extracellular membranous immunoreactivity to BACE501.

Please replace the paragraph at page 26, lines 12-24 with the following replacement paragraph:

In addition to cleaving APP-based substrates, recombinant human BACE also cleaves a substrate with the sequence LVNM/AEGD (SEQ ID NO: 35) (Lin et al. Proc Natl Acad Sci U S A. 97(4):1456-1460 (2000)), a sequence which is the in vivo processing site sequence of human presenilins. Presenilin 1 and presenilin 2 are unstable proteins which are processed and subsequently stabilized by an unknown protease (Capell et al., J. Biol. Chem. 273, 3205 (1998); Thinakaran et al., Neurobiol. Dis. 4, 438 (1998)). It is known that presenilins control the formation of A-β peptide by cleaveage of APP at the gamma-secretase site, but also the activity of BACE. Presenilins therefore enhance the progression of Alzheimer's disease. Thus, the processing of presenilins by BACE would enhance the production of A-β peptide and therefore, further stimulate the progress of Alzheimer's disease. Therefore, a BACE inhibitor would decrease the likelihood of developing or slow the progression of Alzheimer's disease by inhibiting APP cleavage at the beta-secretase site and/(or) by preventing the processing of presenilins, thus indirectly inhibiting APP cleavage at the gamma-secretase site.